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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/077,574	09/24/1998	MICHAEL PANACCIO	DAVIE60001AP	6196

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER

DEVI, SARVAMANGALA J N

ART UNIT PAPER NUMBER

1645

DATE MAILED: 07/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/077,574

Applicant(s)

PANACCIO ET AL.

Examiner

S. Devi, Ph.D.

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 April 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,12,32,33,37,40 and 114-116 ~~is/are~~ are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,2,12,114 and 115 ~~is/are~~ are allowed.
- 6) ☒ Claim(s) 32, 33, 37, 40 and 116 ~~is/are~~ are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

- 1) Acknowledgment is made of Applicants' amendment filed 04/04/05 in response to the non-final Office Action mailed 10/01/04.

Status of Claims

- 2) Claims 1, 2, 12, 32, 37, 40 and 114-116 have been amended via the amendment filed 04/04/05.

Claim 39 has been canceled via the amendment filed 04/04/05.

Claims 1, 2, 12, 32, 33, 37, 40 and 114-116 are pending and are under examination.

Prior Citation of Title 35 Sections

- 3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

- 4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

- 5) The objection to claims 37 and 40 made in paragraph 29 of the Office Action mailed 10/01/04 is withdrawn in light of Applicants' amendment to the claims.

Rejection(s) Moot

- 6) The rejection of claim 39 made in paragraph 26 of the Office Action mailed 10/01/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is moot in light of Applicants' cancellation of the claim.
- 7) The rejection of claim 39 made in paragraph 27 of the Office Action mailed 10/01/04 under 35 U.S.C. § 112, first paragraph, as being non-enabled with regard to the scope, is moot in light of Applicants' cancellation of the claim.

8) The rejection of claim 39 made in paragraph 28 of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

9) The rejection of claims 37 and 40 made in paragraph 26 of the Office Action mailed 10/01/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendment to the claims.

10) The rejection of claims 114-116 made in paragraph 27 of the Office Action mailed 10/01/04 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is withdrawn in light of Applicants' amendment to the claims and/or the base claim.

11) The rejection of claim 1 made in paragraphs 28(a), 28(b) and 28(c) of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

12) The rejection of claim 12 made in paragraph 28(d) of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

13) The rejection of claim 32 made in paragraph 28(e) of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

14) The rejection of claim 40 made in paragraph 28(f) of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

15) The rejection of claim 115 made in paragraph 28(g) of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

16) The rejection of claim 114 made in paragraph 28(h) of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

- 17) The rejection of claim 114 made in paragraph 28(i) of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.
- 18) The rejection of claim 115 made in paragraph 28(j) of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.
- 19) The rejection of claims 40 and 116 made in paragraph 28(k) of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.
- 20) The rejection of claims 2, 12, 32, 33, 37, 40 and 114-116 made in paragraph 28(k) of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

Rejection(s) Maintained

- 21) The rejection of claim 116 made in paragraph 28(f) of the Office Action mailed 10/01/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein. It is noted that Applicants have amended claim 40, but similar amendment has not been made to claim 116.
- 22) The rejection of claims 32, 33, 37 and 40 made in paragraph 27 of the Office Action mailed 10/01/04 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is maintained for reasons set forth therein and herebelow.

With regard to the method for treating an animal infected by *L. intracellularis* as claimed, Applicants present the following arguments: (a) Enablement does not require experimental evidence to prove that a vaccine composition is effective; (b) One of skill in the art knows that currently many vaccines that are administered post-infection are being used very successfully for treatment of many chronic and slow-acting disease, such as rabies; (c) As stated in MPEP 2164.02, compliance with the enablement requirement of 35 U.S.C § 112, first paragraph, does not turn on whether an example is disclosed. An example may be 'working' or 'prophetic'; (d) The specification need not contain an example if the invention is otherwise disclosed in such manner

that one skilled in the art will be able to practice it without an undue amount of experimentation; (e) In the present application, the method of immunizing an animal of claim 32 pre-infection is enabled, and then it follows that the method of treating an animal with a vaccine post-infection is also enabled; (f) The type of vaccine, the amount of vaccine, and the treatment schedule would 'likely' be very close if not identical to that for a pre-infection vaccine; and (g) Undue experimentation would not be necessary to vary the method of immunization pre-infection for a post-infection treatment.

Applicants' arguments have been carefully considered, but are not persuasive. A claim has to be enabled over its full scope. The instant lack of enablement rejection is related to the method of treating an animal infected by *L. intracellularis* comprising administering the composition of claim 1, but not to the method of inducing an immune response against *L. intracellularis* comprising administering the composition of claim 1. An actual working example is not required particularly in an art that is predictable. But in an art where there is unpredictability, evidence enabling the invention is needed. Enablement requires experimental showing that the composition as claimed is effective in treating an already infected animal. The evidence must be either *in vivo* evidence in an accepted animal model, or *in vitro* evidence correlative of therapeutic efficacy. Contrary to Applicants' assertion, whether or not the pigs pre-vaccinated with *L. intracellularis* showed no signs of the disease, PPE, is not relevant to the claimed method of treatment. In the instant Examples, the 'uninfected' pigs were vaccinated with a formalin-killed *L. intracellularis* vaccine. Animals already infected with *L. intracellularis* were not administered with a composition comprising an isolated immunogenic heat shock protein of SEQ ID NO: 2, alone or in combination, with a refolding protein, a flagellar basal body rod protein, an S-adenosylmethionine, tRNA ribosyltransferase-isomerase, an autolysin, an enoyl-(acyl-carrier-protein) reductase, or a glucarate transporter. Immunization of the uninfected animals with a formalin-killed *L. intracellularis* vaccine does not provide enablement for a method of treating an animal infected with *L. intracellularis* comprising administering an 'isolated' protein of SEQ ID NO: 2, with or without, a refolding protein, a flagellar basal body rod protein, an S-adenosylmethionine, tRNA ribosyltransferase-isomerase, an autolysin, an enoyl-(acyl-carrier-protein) reductase, or a glucarate transporter. While induction of an immune response against *L.*

intracellularis in an uninfected animal by a composition comprising an immunogenic heatshock protein of *L. intracellularis* comprising the amino acid sequence of SEQ ID NO: 2 is predictable in this art, a method of treating a *L. intracellularis*-infected animal comprising administration of a composition comprising an immunogenic heatshock protein of *L. intracellularis* comprising the amino acid sequence of SEQ ID NO: 2, with or without another immunogenic component as recited, is not predictable. Despite the level of skill in the art, predictability or unpredictability is also a *Wands* factor for enablement. Absent concrete evidence, there is no predictability that one of skill in the art can successfully apply the claimed method of inducing an immune response against *L. intracellularis* in an uninfected animal to treating animals that are already infected with *L. intracellularis*. There is no showing that the amount of the composition of claim 1 that is effective in inducing an immune response in an uninfected animal is the amount that is effective in treating an already infected animal, whose immune capacity cannot be expected to be same as that of uninfected animals. There is no showing that the routes of administration used in the method of immunization are effectively usable in a method of treatment. There is no showing that morbidity and/or mortality due to *L. intracellularis* were reduced in animals already infected with *L.*

intracellularis following the administration of the composition of claim 1 'in an amount effective to induce an immune response to *L. intracellularis*'. The allegedly successful use of vaccines post-infection for treatment of a disease, such as rabies, is not relevant to the instantly claimed method since infection due to the intracellular *L. intracellularis* bacterial infection and the rabies viral infection are two unrelated infections caused two distinct types of microbes. The invention is not disclosed in a manner that one skilled in the art would be able to practice without a considerable amount of experimentation that is undue. To be enabled, a method of treatment has to use animals already infected by *L. intracellularis* and then administer to the infected animals a therapeutically acceptable amount of the claimed composition comprising the isolated polypeptide of SEQ ID NO: 2, alone or in combination with the recited immunogenic component(s) such that the composition at least reduces, if not eliminates, morbidity and/or mortality due to *L. intracellularis* infection. In the instant case, no animals already infected by *L. intracellularis* have been administered with a composition comprising 'isolated' heat shock protein of SEQ ID NO: 2. There is no showing within the instant specification that the polypeptide in the claimed composition, alone or in

combination with another immunogenic component, induced any therapeutic effects in an animal already infected with *L. intracellularis*. In the instant application, there is neither *in vivo* therapeutic data, nor *in vitro* data correlative of therapeutic protection against *L. intracellularis* infection in any animal, human or non-human. In view of the therapeutic unpredictability, the breadth of the claims, and the amount of experimentation needed, undue experimentation would have been required by one of skill in the art at the time of the instant invention. The rejection stands.

New Rejection(s) Based on Applicants' Amendment

The new rejection(s) set forth below are necessitated by Applicants' amendments to the claims.

Rejection(s) under 35 U.S.C. 112, Second Paragraph

23) Claims 32, 33, 37 and 40 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 32 is vague and indefinite in the recitation: method for treating an animal comprising administering ... the composition of Claim 1 'in an amount effective' to induce an immune response to *L. intracellularis*'. It is unclear how an amount of the composition that is effective to 'induce an immune response' to *L. intracellularis* in an animal would 'treat' an animal infected by *L. intracellularis*.

(b) Claim 40 lacks proper antecedent basis in the limitation 'at least one immunogenic component' (see line 2). Claim 40 depends from claim 37, which already recites 'immunogenic component'. For clarity, for the purpose of distinctly claiming the subject matter and/or for proper antecedence, it is suggested that Applicants replace the limitation 'comprises more than one immunogenic component' in line 2 of claim 37 with --further comprises at least one immunogenic component-- and replace the limitation 'at least one immunogenic component' in line 2 of the dependent claim 40 with 'said at least one immunogenic component--'.

(c) Claims 33 and 37, which depend from claim 32, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Remarks

24) Claims 1, 2, 12, 114 and 115 are allowable. Claims 32, 33, 37, 40 and 116 stand rejected.

25) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

26) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Central Fax number for submission of amendments, response and papers is (703) 872-9306.

27) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail service. The Examiner can normally be reached on Monday to Friday from 7.15 a.m to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

June, 2005